REMARKS/ARGUMENT

Claims 15-21 were rejected under 35 U.S.C. § 112, second paragraph for being indefinite with regard to whether the effective amount referred to the first composition, second composition or a combination. Claim 15 was intended to be parallel to Claim 1 (where no such rejection was made) and has now been amended so as to be consistent with Claim 1. Claim 20 was also intended to parallel Claim 1 but specify that the ammonium material was ammonium chloride and the claim has converted into dependent form so as to be more clear as to this point. In light of the these amendments, it is respectfully submitted that the Section 112 rejection can now be withdrawn.

Claim 15 has been further amended to specify the amounts of infusion previously recited in Claims 7 and 9. As a result, it is respectfully submitted that the rejection of Claims 15-19 under 35 U.S.C. § 102 over Veech has been rendered moot and should be withdrawn.

Claims 1, 2 and 4-14 have been rejected under 35 U.S.C. § 103 over Feliciano in view of Weisiger and "applicant's admissions" while Claims 20 and 21 have been rejected under 35 U.S.C. § 103 over Veech in view of "applicant's admissions". Both of these rejections are respectfully traversed.

The newly cited Feliciano article is concerned with the Top 10 Supplements for Bodybuilders. The article indicates that the calcium, magnesium and potassium salts of alpha-ketoglutarate have been demonstrated to increase muscle glutamine stores in severely catabolic hospital patients to a greater degree than leucine without indicating how much greater or to what extent leucine increases muscle glutamine stores. The article does not teach the use of an ammonium material for any purpose or, as the Examiner has acknowledged, teach the incorporation of ammonia along with alpha-ketoglutarate. It also does not teach dosing rates. In considering the rejection, it is important to recognize that Feliciano teaches the combination of

alpha-ketoglutarate with KIC (ketoisocaporate) and leucine produces strong anti-catabolic effects.

The Weisiger article is concerned with hepatic metabolism in liver disease. The last paragraph on page 77 noted by the Examiner indicates that an important hepatic detoxification pathway converts ammonium ion to urea through the Krebs-Henseleit urea cycle. The article further teaches that 25% of the abundant amounts of ammonia formed in the intestinal tract by bacterial degradation of luminal (food) peptides, proteins and urea reach the liver where it is detoxified to urea. In a condition where this important detoxification process fails, ammonium ion may enter the peripheral circulation and cause life threatening conditions like hepatic encephalopathy. It will be appreciated that in this context, Weisiger considers ammonia to be a toxin. Weisiger, therefore, teaches away from the present invention. Because of this, the combination of Feliciano and Weisiger would not lead one skilled in the art to the present invention.

"Applicant's admissions" do not cure this deficiency. It is indicated on page 2 of the application that ammonium is "occasionally" administered to patients in spite of it being considered neurotoxic. It is further stated that it causes metabolic acidosis when it is given by slow infusion in the form of the chloride in severe metabolic alkalosis. The so-called "admissions" essentially confirm the teachings of Weisiger but additionally point out the bad effects given when ammonium is infused. It is further respectfully submitted that the assertion in the Office Action that ammonium chloride is known to be administered to patients is not an accurate recitation of what Applicant in fact teaches and when the actual teaching is considered, that teaching, like Weisiger, teaches away from the present invention.

In light of the foregoing considerations, it is respectfully submitted that the rejection based on these two references should be withdrawn.

The Veech Patent has been discussed in the previous response and that discussion is incorporated herein by reference. The additional reliance on applicant's so-called "admissions" is respectfully submitted to be improper and insufficient for the reas ns set forth above. Accordingly, it is respectfully submitted that the rejection based on Veech and the admissions should also be withdrawn.

In light of all of the foregoing, it is respectfully submitted that this application is now in condition to be allowed an the early issuance of a Notice of Allowance is respectfully requested.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Asst. Commissioner for Patents, Washington, D.C. 20231, on December 13, 2001:

Edward A. Meilman
Name of applicant, assignee or Registered Representative

Signature

December 13, 2001
Date of Signature

EAM:sds:mgs

Respectfully submitted,

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APPENDIX A

"CLEAN" VERSION OF EACH PARAGRAPH/SECTION/CLAIM
37 C.F.R. § 1.121(b)(ii) AND (c)(i)

CLAIMS (with indication of amended or new):

(Amended) 15. A pharmaceutical dosage unit comprising a first pharmaceutical composition comprising at least one of α-ketoglutarate and α-ketoglutaric acid in a pharmaceutically acceptable carrier and a second pharmaceutical composition comprising ammonium in a pharmaceutically acceptable carrier, the total amount of the at least one of α-ketoglutarate and α-ketoglutaric acid and the ammonium being effective to preserve skeletal muscle, and wherein the amount of infusion administrated of said at least one of α-ketoglutarate and α-ketoglutaric acid is from 0.02 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 30 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ and the amount of infusion administrated of NH_4^+ is from 0.5 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 20 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

(Amended) 20. The method of 1, wherein the ammonium is ammonium chloride.

APPENDIX B

VERSION WITH MARKINGS TO SHOW CHANGES MADE
37 C.F.R. § 1.121(b)(iii) AND (c)(ii)

CLAIMS:

15. A pharmaceutical dosage unit comprising a first pharmaceutical composition comprising at least one of α-ketoglutarate and α-ketoglutaric acid in a pharmaceutically acceptable carrier and a second pharmaceutical composition comprising ammonium in a pharmaceutically acceptable carrier, the total amount of the at least one of α-ketoglutarate and α-ketoglutaric acid and the ammonium being [in an amount] effective to preserve skeletal muscle, and wherein the amount of infusion administrated of said at least one of α-ketoglutarate and α-ketoglutaric acid is from 0.02 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 30 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ and the amount of infusion administrated of NH_4^+ is from 0.5 $\mu mol \cdot kg^{-1} \cdot min^{-1}$ to 20 $\mu mol \cdot kg^{-1} \cdot min^{-1}$.

20. [A] The method of [preserving bodily protein stores in a catabolic patient, comprising the concomitant administration (a) at least one of α-ketoglutarate and α-ketoglutaric acid and (b)] 1, wherein the ammonium is ammonium chloride [in an amount effective to preserve skeletal muscle].